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PTO/SB/33 (07-09)
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PRE-APPEAL BRIEF REQUEST FOR REVIEW

Docket Number (Optional): 207,380

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Application Number	Filed
10/561,670	December 19, 2005

First Named Inventor: Franco Macchi

Art Unit	Examiner
1623	BLAND, Layla D.

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

☐ applicant/inventor.

☐ assignee of record of the entire interest.
See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed.
(Form PTO/SB/96)

☑ attorney or agent of record.
Registration number 24,156.

☐ attorney or agent acting under 37 CFR 1.34.
Registration number if acting under 37 CFR 1.34 _____

/Jay S. Cinamon/
Signature

Jay S. Cinamon
Typed or printed name

212-885-9232
Telephone number

June 1, 2011
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required.
Submit multiple forms if more than one signature is required, see below*.

☑ *Total of 3 forms are submitted.

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s):	Macchi	Confirmation No.:	5848
Serial No.:	10/561,670	Art Unit:	1623
Filed:	December 19, 2005	Examiner:	BLAND, Layla D.
		Attorney Docket No.:	207,380

Title: USE OF HYALURONIC ACID FOR PREPARING COMPOSITIONS FOR TREATING ORAL CAVITY APHTHAS

PRE-APPEAL BRIEF REQUEST FOR REVIEW

TO THE COMMISSIONER FOR PATENTS:

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with his request. This request is being filed with a Notice of Appeal.

The review is requested for the reason(s) stated below, and no more than five (5) pages have been provided.

Claims 7-13 are pending and stand rejected. Briefly, Claim 7 is directed to a method for the treatment of Recurrent Oral Aphthous Ulcers (ROAU) comprising administering, as the sole active ingredient, hyaluronic acid or a salt thereof, having an average molecular weight comprised between 800,000 and 4,000,000, to a subject in need thereof. Claims 8, 12 and 13 depend from Claim 7, Claim 9 depends from Claim 8, Claim 10 depends from Claim 9, and Claim 11 depends from Claim 10.

Claims 7-13 are rejected under 35 U.S.C. § 103(a) as obvious over Di Schiena (European Patent No. EP 0444492) in view of Saxen (Saxen et al., Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1997; 84:356-61).

1. **Di Schiena in view of Saxen, Fails to Teach or Suggest Every Limitation of the Claimed Invention**

   (i) Saxen fails to teach or suggest that hyaluronic acid (HA), as the sole active ingredient, is useful for therapy of RAS.

The Examiner improperly supports the obviousness rejection over Di Schiena in view of Saxen and fails to show that the claimed invention is taught or suggested by the art.

The Examiner states that *Di Schiena teaches pharmaceutical compositions comprising 0.2 to 10% sodium hyaluronate having molecular weight between 800,000-4,000,000, preferably 1,000,000-2,000,000 for the treatment and prophylaxis of inflammatory affections of the oral cavity.*

The Examiner also affirms that *Di Schiena does not exemplify the treatment of recurrent oral aphthous ulcers using the composition.*

In the Office Action of February 3, 2011 ("O.A.6"), page 3, par.1, the Examiner affirms (and already indicated in the Office Action of March 9, 2009 ("O.A.3") page 6, par.3) that: *Saxen teaches that recurrent aphthous ulcers are a common disorder, causing pain from inflammatory sensitization of nerve endings.... Adults having aphthous ulcers were treated with 3% diclofenac in 2.5% hyaluronan, 2.5% hyaluronan or 3% viscous lidocaine. A 48% reduction in pain was observed 10 minutes after application with no significant difference between the three topical agents [see abstract].*

The distinguishing features of the method as recited in present Claim 7 are:

- the pathology to be treated: recurrent oral aphthous ulcers (ROAU);
- **the sole active ingredient: hyaluronic acid;**
- the average molecular weight of the hyaluronic acid: comprised between 800,000 and 4,000,000.

In contrast to these distinguishing features, Saxen teaches that **hyaluronan (HA) alone** is **not effective** on ROAU. In fact in Applicant's response of September 26, 2008 ("Resp.2") page 5, last par., Applicant points out that the Examiner's affirmations are incorrect since she relies on the abstract of Saxen on which to base her reasoning.

Applicant reiterated this in the Response of July1, 2009 ("Resp3") page 6, in the Response of April 20, 2010 ("Resp.4") pages 4-5, and also in the Response of January 4, 2011 ("Resp.5") page 2, last two paragraphs.

Applicant pointed out that this basis is not correct because the data for the reduction of 48% in pain refers only to the preparation of diclofenac/HA as clearly stated at page 359, 1st column, lines 5-9, wherein it is stated that for diclofenac/HA a highly significant effect was observed and *"neither lidocaine nor hyaluronan were significantly different from baseline pain level"*.

Therefore, the abstract of Saxen, if read correctly and in its entirety, does not teach that HA would be useful for the treatment of recurrent oral aphthous ulcers, but that **diclofenac/HA** gel can be used in the treatment.

To the extent the Examiner mistakenly relies upon this section of Saxen to support the obviousness rejection, the rejection is improper.

Applicant furthermore underscores the fact that there is no teaching in Saxen that HA is effective for the treatment of ROAU and that, on the contrary, as explained in Resp.5, page 2, par.4, Saxen reports that "*A 35% to 52% pain reduction ($p<0.01$) was reported 2 to 6 hours after the application of diclofenac in hyaluronan, while hyaluronan gel alone and viscous lidocaine **failed** to produce significant VAS reduction*" (emphasis added).

Failing to consider references as a whole in making an obviousness rejection is an error on the part of the Examiner (M.P.E.P.§2141.02) and, therefore, the rejection cannot stand.

Saxen fails to teach that HA alone is effective in the treatment of ROAU, a pathology of unknown origin and which is very difficult to treat, and the obviousness rejection is therefore improper to the extent that the Examiner relies upon the abstract of Saxen to support the obviousness rejection.

(ii) Saxen fails to teach or suggest that hyaluronic acid (HA) is an active principle.

In O.A.6, page 4, last 3 lines of par.2, the Examiner affirms that *based on Saxen's teaching alone, the skilled artisan would conclude that HA alone is effective for short-term pain relief due to oral aphthous ulcers.*

In the Office Action of July 7, 2010 ("O.A.5"), page 5, last 2 lines of par.3, the Examiner states that *even if Saxen is interpreted to suggest only immediate pain relief, pain management is the common treatment for ROAU, as taught by Saxen.* Applicant contests this affirmation, which is the Examiners' deduction since Saxen states at page 360, 1st column, beginning of par..3 "the ***blunting action** of hyaluronan*, an agent with ***no know analgesic or anaesthetic activity***...."(emphasis added) and after a comparison with carboxymethylcellulose in the following paragraph states that HA is "a similar, ***pharmacologically inert agent***"(emphasis added).

How could HA be used for the treatment of a pathology if the teaching of Saxen is that HA is a pharmacologically inert agent? Saxen fails to teach that *"HA alone can be used to treat recurrent aphthous ulcers*" (O.A.6, page 3,lines 5-6 of Par.2). This rejection is improper since a ***pharmacologically inert agent*** is not equivalent to an agent which is used to treat a pathology. This interpretation is corroborated throughout Saxen, for example at page 356, 2nd column, last two lines "ability of the **hyaluronan vehicle** to transport diclofenac" (emphasis added).

Saxen therefore fails to teach that HA alone can be used to treat ROAU, and the obviousness rejection is improper in view of the Examiner's misinterpretation of the teaching of Saxen.

(iii) Saxen fails to teach or suggest that hyaluronic acid (HA) is effective in the reduction of lesion size.

In the Office Action of October 21, 2009 ("O.A.4), page 5, last paragraph, the Examiner affirms that "*Table 1 clearly teaches that there was a reduction in lesion size. The maximum lesion size went from 9 to 6, a 30% reduction, and the smallest ulcer size went from 3 to 0.*".

Applicant explained in Resp.4, page 5 and reiterated this argument in Resp.5, page 3, par. 5, that: Table 1 of Saxen, indicates demographic characteristics of the treatment groups, that Table 1 clearly indicates p value of the lesion size, which are not significant, and most importantly that this is **confirmed by Saxen** himself, who stated "*No significant change in ulcer diameter or clinical appearance of the ulcer was observed throughout of the trial.*" Page 358, 2nd column, lines 9-11 of last paragraph.

Since Saxen fails to teach that HA is effective in the reduction of lesion size, the skilled person having read Saxen would, without doubt, be led to ***disregard its teachings*** and would not be encouraged to use HA for reducing mouth lesions with a reasonable expectation of achieving the desired result. To the extent the Examiner erroneously reads the explicit teachings of the prior art, relies upon Table 1 to support the obviousness rejection, and asserts that this reference reads on the present claims, the rejection is improper.

Since the teachings of Saxen fail to cure the deficiencies of Di Schiena teachings for achieving the objectives of the claimed invention, the obviousness rejection is unsupported.

Conclusion

In view of the foregoing remarks, and as supplemented by Applicant's responses of record, the pending claims clearly distinguish over the combined teachings of Di Schiena in view of Saxen.

Withdrawal of the obviousness rejection is, therefore, respectfully solicited.

Please charge any fees which may be due and which have not been submitted herewith to our Deposit Account No. 01-0035.

Respectfully submitted,

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Date June 1, 2011

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